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Post-Bariatric Surgery Liver Injury Assessment Using Circulating Caspase-Cleaved Keratin 18

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Abstract

Bariatric surgery is now recognized as a powerful therapeutic approach for individuals with morbid obesity who also suffer from non-alcoholic fatty liver disease (NAFLD). Despite its metabolic benefits, postoperative progression or new emergence of non-alcoholic steatohepatitis (NASH) and hepatic fibrosis has occasionally been reported. Caspase-cleaved keratin 18 (ccK18), a byproduct of hepatocyte apoptosis, has been identified as a reliable indicator of liver cell death—an essential process in NASH pathogenesis. Therefore, serial ccK18 testing could serve as a practical tool for tracking hepatic recovery in post-bariatric patients. In this study, clinical and biochemical data were obtained from 39 individuals who underwent laparoscopic Roux-en-Y gastric bypass, assessed across six timepoints from baseline to one year post-surgery. Serum ccK18 concentrations were determined, and large-scale profiling of circulating adipokines and cytokines was performed. Half of the participants (20 of 39) exhibited ccK18 values suggestive of advanced liver injury, while 21% had NAFLD fibrosis scores exceeding 0.676, consistent with significant fibrosis. After one year, patients experienced an average body weight reduction of 36.87%. At both six and twelve months after surgery, ccK18 fragment levels declined markedly compared to preoperative measurements ($p < 0.001$). Yet, nine subjects failed to reach at least a 10% drop in ccK18 over the same period, categorizing them as non-responders. Although standard laboratory indices and mean ccK18 values did not differ significantly, these non-responders exhibited higher baseline levels of leptin and fibrinogen. Sequential ccK18 evaluation effectively tracked NAFLD remission and identified patients with unresolved liver damage after bariatric surgery. Additional investigations are required to clarify the mechanisms underlying poor hepatic recovery and to evaluate the prognostic use of adipokines in this setting.

Keywords: Non-alcoholic fatty liver disease, NAFLD, NASH, Keratin 18, cytokeratin 18, M30, Gastric bypass, Non-invasive biomarkers

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Introduction

Non-alcoholic fatty liver disease (NAFLD) represents the hepatic aspect of the broader metabolic syndrome and encompasses a continuum ranging from benign steatosis to inflammatory non-alcoholic steatohepatitis (NASH), cirrhosis, and even hepatocellular carcinoma (HCC) [1,2]. It has become one of the most prevalent chronic liver conditions worldwide and is increasingly recognized as a leading cause of hepatic failure, liver cancer, and transplantation [3,4]. Despite major progress in

uncovering its multifactorial pathogenesis, no pharmacologic therapy has yet been approved for NAFLD [5]. Treatment strategies remain centered on correcting metabolic disturbances, with bariatric surgery emerging as a highly effective intervention in patients with severe obesity [6–8]. Global clinical guidelines now recommend surgical treatment when lifestyle-based methods fail to achieve sufficient improvement [9–12].

At the same time, NAFLD occurs frequently among bariatric candidates [13–15], emphasizing the need for dedicated liver evaluation before and after surgery. This is particularly crucial since some reports have documented disease progression or de novo development of NASH and fibrosis following surgery. A meta-analysis has shown this in roughly 5–20% of cases [8]. Because most of these investigations rely on serial liver biopsies—the current but invasive diagnostic benchmark—their use is limited by risk, expense, sampling errors, and interpretation variability. Consequently, there is a strong demand for reliable non-invasive biomarkers to allow consistent hepatic monitoring in these patients.

Among potential candidates, caspase-cleaved keratin 18 (ccK18) has gained significant attention. During programmed hepatocyte death, fragments of ccK18 enter the bloodstream and can be quantified using the M30 enzyme-linked immunosorbent assay (ELISA) [16,17]. Elevated circulating ccK18 has been associated with various chronic liver disorders [18,19], and since apoptosis plays a central role in NAFLD progression, this marker has been widely examined as a non-invasive diagnostic tool [20–27]. Studies have shown moderate diagnostic performance, and ccK18—alone or as part of multimarker panels—is anticipated to be incorporated into future clinical workflows [28,29]. Moreover, its sensitivity to both pharmacological and dietary interventions has been verified in previous trials [30–32].

Based on these findings, monitoring ccK18 may provide an efficient means of evaluating hepatic recovery and treatment response following bariatric surgery. The present study aimed to determine:

(1) the baseline prevalence of NAFLD as reflected by ccK18 levels and fibrosis scores before and after surgery;

(2) the longitudinal pattern of ccK18 following bariatric intervention; and

(3) whether a subset of patients fails to respond biochemically—and if incorporating ccK18 into postoperative follow-up panels could help predict these cases.

Materials and Methods

Patient selection

Serum and clinical information were gathered from a continuous series of individuals who underwent laparoscopic Roux-en-Y gastric bypass (RYGB) at the University of Giessen's Obesity Center in Germany. Surgical eligibility followed current clinical standards: a body mass index (BMI) exceeding 40 kg/m², or ≥ 35 kg/m² accompanied by type 2 diabetes mellitus; unsuccessful conservative weight reduction; and no medical contraindications. Anyone with a previous bariatric procedure was not considered. Each participant's medical background was reviewed, and all underwent clinical assessment. Written informed consent was obtained before inclusion. Ethical clearance was provided by the Justus Liebig University ethics board (approval no. AZ 60/16). All procedures complied with the Declaration of Helsinki.

Surgical technique

All bypass operations were executed by a single senior surgeon in a tertiary medical facility within a multidisciplinary program. The technique consisted of a gastric bypass with a concurrent fundectomy, followed by circular gastrojejunostomy construction. The created pouch measured approximately 8–10 cm. The biliopancreatic and alimentary limbs were fashioned with lengths of 70–90 cm and 140–160 cm, respectively.

Data recording and Follow-Up

Participants were evaluated at six fixed intervals: several days prior to surgery, 1–3 days afterward, and at 1, 3, 6, and 12 months post-operation. At each timepoint, body composition data and a full laboratory profile were documented. Extra blood samples for measuring ccK18 were obtained either during follow-up appointments or provided by the Institute of Laboratory Medicine. At two stages—before surgery and at month 6—samples were taken both fasting and after consumption of a standardized meal.

Measurement of ccK18 in serum

Serum ccK18 was quantified using the Peviva® M30 Apoptosense® ELISA (TECOmedical, Sissach, Switzerland). Each sample was analyzed twice following the manufacturer's specifications. Concentrations were calculated using an Infinite® 200 Pro plate reader together with Magellan™ software (TECAN, Männedorf, Switzerland) using a four-parameter logistic fit.

Classification of responders

Patients were categorized according to the change in ccK18 over one year. A decrease of ≥ 10% relative to baseline was interpreted as biochemical improvement and defined as a *response* to surgery. Allocation into "responder" or "non-responder" groups was performed based on this cutoff for later comparisons.

Protein array analysis

To explore circulating proteins linked to metabolic change, pooled serum from nine responders and nine non-

responders was analyzed both pre-surgery and one year afterward using the Human Adipokine and Cytokine Array Kits (ARY024 and ARY005B; R&D Systems, Minneapolis, MN, USA). Experimental processing followed established methods [33]. Average grey intensities were normalized against positive controls, and relative signal shifts between the two timepoints were determined for each protein.

Statistical evaluation

All datasets, fibrosis scores, and descriptive summaries were compiled with SPSS Statistics v25 (IBM, Armonk, NY, USA). Further statistical tests were performed using Prism 8 for macOS (v8.4.3; GraphPad, La Jolla, CA, USA). To analyze longitudinal changes, a mixed-effects model with Geisser–Greenhouse correction was applied, addressing repeated measures. Two-way ANOVA was employed to compare responders and non-responders at each timepoint, followed by Sidak's post-hoc multiple-comparison test. A p-value < 0.05 was regarded as statistically significant.

Results

Characteristics prior to surgery

Thirty-nine individuals were enrolled. Their demographic and clinical data are presented in **Table 1**. The majority were women, aged 23–60 years. Every participant was classified as morbidly obese (BMI > 40 kg/m²) with a mean BMI of 51.94 kg/m² before surgery. None had a confirmed diagnosis of chronic liver disease. However, several had metabolic comorbidities such as diabetes or glucose intolerance, dyslipidemia, and elevated hepatic enzymes **(Table 1)**, all of which are strong indicators of NAFLD risk.

Roughly half of the cohort (20 out of 39) exhibited ccK18 concentrations exceeding 200 U/L, levels previously associated with advanced hepatic injury [18, 24, 25]. To further estimate fibrosis probability, non-invasive indices were calculated. Very few participants crossed the diagnostic thresholds of the APRI or FIB-4 scores [34, 35], yet approximately 21% had a NAFLD Fibrosis Score (NFS) > 0.676, reflecting possible stage 3–4 fibrosis [36].

Table 1. Baseline characteristics of all participants before and one year following RYGB

Parameter	Preoperative (n = 39)	1 Year Postoperative (n = 39)	p-value (Adjusted)
Demographics			
Age (years)	39.44 (23 to 60)		
Female gender	35 (90%)		
Anthropometric Measures			
BMI (kg/m²)	51.94 (41.56 to 61.85)	32.64 (17.88 to 54.37)	<0.001
Body weight (kg)	146.54 (111.7 to 190.5)	91.84 (61.3 to 125)	<0.001
Total body weight loss (%)		36.87 (17.88 to 54.37)	
Excess weight loss (%)†		71.89 (38.64 to 105.29)	
Metabolic Parameters			
HbA1c (%)	6.19 (4.7 to 9.6)	5.29 (4.5 to 6.7)	<0.001
Diabetes mellitus	10 (31%)	2 (5%)	
LDL cholesterol (mg/dL)	129.65 (53 to 233)	91.92 (20 to 153)	<0.001
HDL cholesterol (mg/dL)	46.32 (27 to 87)	50.79 (17 to 95)	0.021
Serum triglycerides (mg/dL)	173.12 (58 to 751)	88.1 (44 to 253)	<0.001
CRP (mg/L)	17.72 (2.09 to 146.61)	1.87 (0.5 to 14.6)	0.004
Liver Function Tests			
Log ccK18 (U/L)	2.37 (2.01 to 3.17)	2.09 (1.64 to 2.62)	<0.001
ccK18 > 200 U/L	20 (51%)	5 (13%)	
ALT (U/L)	41.03 (11 to 126)	36.15 (10 to 186)	0.914
AST (U/L)	31.15 (10 to 136)	23.44 (8 to 137)	0.285
Alkaline phosphatase (U/L)	77.44 (48 to 114)	82.74 (43 to 270)	0.836
GGT (U/L)	41 (9 to 162)	23.26 (6 to 279)	0.280
Bilirubin (mg/dL)	0.49 (0.3 to 1)	0.58 (0.2 to 1.5)	0.024
Albumin (g/dL)	4.29 (3.61 to 5.1)	4.41 (3.92 to 5)	0.213
Fibrosis Assessment			
NFS	−0.24 (−3.01 to 2.78)	−2.36 (−5.44 to 0.4)	<0.001
NFS > 0.676	8 (21%)	0	
APRI	0.29 (0.06 to 0.99)	0.24 (0.05 to 1.25)	0.576
APRI > 0.7	2 (5%)	1 (3%)	
FIB-4	0.71 (0.23 to 1.67)	0.63 (0.21 to 1.51)	0.311
FIB-4 > 3.25	0	0	

Data are expressed as mean (range) or n (%). † Excess body weight was estimated relative to a BMI of 25. Abbreviations: BMI, body mass index; LDL, low-density lipoprotein; HDL, high-density lipoprotein; CRP, C-reactive protein; ccK18, caspase-cleaved keratin 18 (M30); ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; NFS, NAFLD fibrosis score; APRI, AST-to-platelet ratio index.

Roux-en-Y gastric bypass resulted in substantial weight reduction and metabolic benefits

Every participant experienced a gradual and continuous loss of body mass after the bariatric operation **(Figure 1A, B)**. Twelve months post-surgery, the mean total body

weight loss (TBWL) reached 36.87% (95% CI: 34.16–39.57%), with an excess weight loss (EWL) of 71.89% (66.87–76.91%) **(Table 1)**. The average BMI dropped to 32.64 (95% CI 31.38–34.1). The outcomes were consistent across all subjects, and the smallest individual TBWL recorded was 17.88%. Alongside the reduction in weight, notable improvements occurred in metabolic indicators such as HbA1c, LDL-cholesterol, and triglycerides **(Table 1)**.

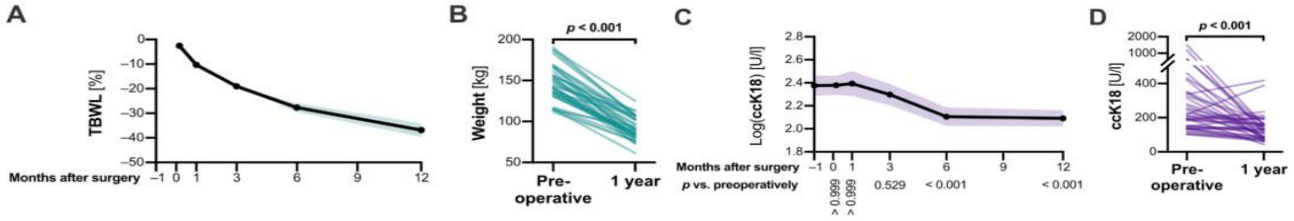

Figure 1. Roux-en-Y gastric bypass caused reductions in both body mass and circulating caspase-cleaved keratin 18. (A) Weight declined steadily after surgery, with a mean TBWL of approximately 37% by the one-year mark. The mean (solid line) and 95% confidence interval (shaded zone) are presented. (B) Compared with preoperative levels, this decrease was highly significant ($p < 0.001$). (C) Serum ccK18 fragments, quantified using an M30 ELISA, fell significantly within six months following surgery. (D) Nevertheless, the individual progression of ccK18 values differed between patients. Data were modeled using a mixed-effects approach

Reduction in ccK18 detected within six months after surgery

Serum samples were obtained at six defined intervals—from several days prior to the procedure up to one year later—to evaluate the trend in ccK18 concentrations. Whether blood was collected fasting or non-fasting did not influence the outcome; coefficients of variation at two sampling points were 8.15% and 8.68%, both below the manufacturer's stated inter-assay limit of <10% (Supplementary Figure S1). Because the ccK18 data followed a lognormal curve, logarithmic transformations were applied in further analyses. During the initial postoperative month, ccK18 means remained stable (Figure 1C). However, by six and twelve months, levels had fallen markedly relative to baseline ($p < 0.001$). This pattern contrasted with that of liver injury enzymes (ALT, AST, GGT), which first rose shortly after the operation and subsequently normalized (Figure S2). At one year, only 5 of 39 subjects maintained ccK18 concentrations above 200 U/l **(Table 1)**.

Variation in individual response to bariatric surgery

Analysis of patient-specific trajectories revealed that not everyone experienced a postoperative drop in ccK18 **(Figure 1D)**. This observation aligns with earlier biopsy-based research, where 5–20% of individuals showed either new or aggravated NAFLD following bariatric procedures [8]. In this cohort, ccK18 changes were not significantly correlated with total weight loss ($r = 0.32$, $p = 0.05$, **Figure 2A**) or excess weight loss ($r = 0.12$, $p = 0.462$, **Figure 2B**). Some patients achieved ccK18 regression with as little as a 20% decrease in weight. To assess clinical response, participants were classified as responders when ccK18 dropped by ≥10% one year after surgery relative to baseline. Out of 39 individuals, 30 met this threshold **(Figure 2C)**. Responders and non-responders were compared to determine whether ccK18, when analyzed with standard biochemical markers, could serve as a predictor of surgical outcome. Results **(Table 2)** indicated that pre-surgery triglyceride levels were significantly higher in responders (+42.33 mg/dl, 95% CI 1.4–83.25 mg/dl, $p = 0.036$), whereas non-responders exhibited elevated GGT at follow-up (+44.3 U/l, 95% CI 21.21–67.39 U/l, $p < 0.001$).

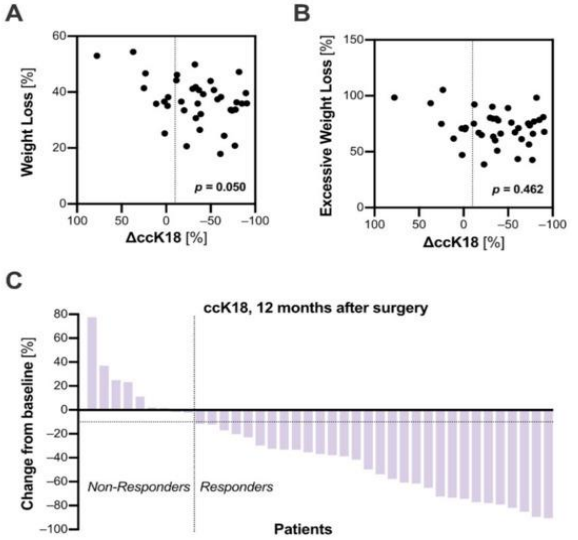

Figure 2. Sequential assessment of ccK18 levels revealed patients unresponsive to bariatric surgery. The individual variations in ccK18 concentration over the 12-month follow-up period (ΔccK18) showed no clear correlation with either (A) total body weight reduction ($r = 0.32$) or (B) excess weight loss ($r = 0.12$). Excess weight loss was determined using a reference BMI of 25. The analysis employed Spearman's correlation coefficient. Panel (C) illustrates a waterfall plot, presenting the change in ccK18 levels for each patient one year post-surgery in comparison with baseline. Although the majority demonstrated a decline, some participants exhibited unchanged or elevated

ccK18 concentrations. For subsequent evaluations, participants were divided into "Responders" and "Non-Responders", where response was defined as a ≥10% reduction in ccK18 levels one year after surgery

Table 2. Comparative characteristics of responders and non-responders before and one year after bariatric surgery

Parameter	Preoperative			1 Year Postoperative		
	Responders (n = 30)	Non-Responders (n = 9)	p-value (Adjusted)	Responders (n = 30)	Non-Responders (n = 9)	p-value (Adjusted)
Demographics						
Age (years)	39.1 (23 to 60)	40.56 (27 to 51)	>0.999			
Female gender	27 (90%)	8 (89%)				
Anthropometric Measures						
BMI (kg/m²)	51.4 (41.56 to 61.85)	53.72 (44.92 to 59.88)	>0.999	32.89 (25.4 to 42.52)	31.81 (23.95 to 40.15)	>0.999
Body weight (kg)	145.51 (111.7 to 190.5)	149.98 (115 to 183)	>0.999	92.79 (73.4 to 125)	88.68 (61.3 to 108)	>0.999
Metabolic Parameters						
Diabetes mellitus	8 (33%)	2 (25%)		1 (3%)	1 (11%)	
LDL cholesterol (mg/dL)	128.15 (53 to 233)	134.5 (90 to 165)	>0.999	90.63 (20 to 145)	96.22 (65 to 153)	>0.999
HDL cholesterol (mg/dL)	44.5 (27 to 71)	52.25 (31 to 87)	>0.999	49.3 (17 to 83)	55.78 (38 to 95)	>0.999
Serum triglycerides (mg/dL)	183.08 (58 to 751)	140.75 (98 to 189)	0.036	90.53 (44 to 253)	80 (44 to 120)	0.962
CRP (mg/L)	15.25 (2.09 to 146.61)	25.94 (8.12 to 110.89)	>0.999	1.26 (0.5 to 7.91)	3.9 (0.5 to 14.6)	>0.999
Liver Function Tests						
Log ccK18 (U/L)	2.4 (2.01 to 3.17)	2.27 (2.13 to 2.53)	>0.999	2.02 (1.64 to 2.28)	2.34 (2.21 to 2.62)	>0.999
ccK18 > 200 U/L	17 (57%)	3 (33%)		0	5 (56%)	
ALT (U/L)	45.5 (11 to 126)	26.11 (13 to 43)	0.921	34.47 (10 to 186)	41.78 (10 to 102)	>0.999
AST (U/L)	34.13 (10 to 136)	21.22 (12 to 30)	>0.999	22.87 (8 to 137)	25.33 (12 to 42)	>0.999
Alkaline phosphatase (U/L)	76.87 (48 to 114)	79.33 (50 to 114)	>0.999	78.27 (43 to 122)	97.67 (60 to 270)	0.194
GGT (U/L)	45.33 (9 to 162)	26.56 (11 to 56)	0.939	13.03 (6 to 40)	57.33 (10 to 279)	<0.001
Bilirubin (mg/dL)	0.49 (0.3 to 1)	0.5 (0.3 to 0.7)	>0.999	0.59 (0.2 to 1.5)	0.54 (0.3 to 0.9)	>0.999
Albumin (g/dL)	4.35 (3.8 to 5.1)	4.09 (3.6 to 4.6)	>0.999	4.47 (4.03 to 5)	4.24 (3.92 to 4.5)	>0.999
Fibrosis Assessment						
NFS	−0.27	−0.164	>0.999	−2.21 (−4.68 to 0.4)	−2.87 (−5.44 to −0.44)	>0.999
NFS > 0.676	6 (20%)	2 (22%)		0	0	
APRI	0.318	0.187	>0.999	0.24 (0.05 to 1.25)	0.23 (0.09 to 0.48)	>0.999
APRI > 0.7	2 (7%)	0		1 (3%)	0	
FIB-4	0.74	0.594	>0.999	0.64 (0.21 to 1.51)	0.59 (0.36 to 1.33)	>0.999
FIB-4 > 3.25	0	0		0	0	

Data are displayed as Mean or Median (range), or n (%).

Abbreviations: LDL – low-density lipoprotein; HDL – high-density lipoprotein; CRP – C-reactive protein; ccK18 – caspase-cleaved keratin 18 (M30); ALT – alanine aminotransferase; AST – aspartate aminotransferase; GGT – gamma-glutamyl transferase; NFS – NAFLD fibrosis score; APRI – AST-to-platelet ratio index.

Adipokine and cytokine profiles differentiated responders from non-responders

We next examined whether molecular patterns of adipokines and cytokines could distinguish patients who responded to bariatric surgery from those who did not. Before the operation, non-responders exhibited markedly higher fibrinogen expression, which was almost undetectable in the responder group **(Figure 3A,B)**. Additionally, non-responders showed 14% greater leptin levels and a 25.6% reduction in nidogen-1 expression. Serial adipokine profiling demonstrated opposing

postoperative trends for fibrinogen and insulin-like growth factor binding protein 6 (IGFBP-6) **(Figure 3C)**: both proteins increased in responders but declined in non-responders one year after surgery.

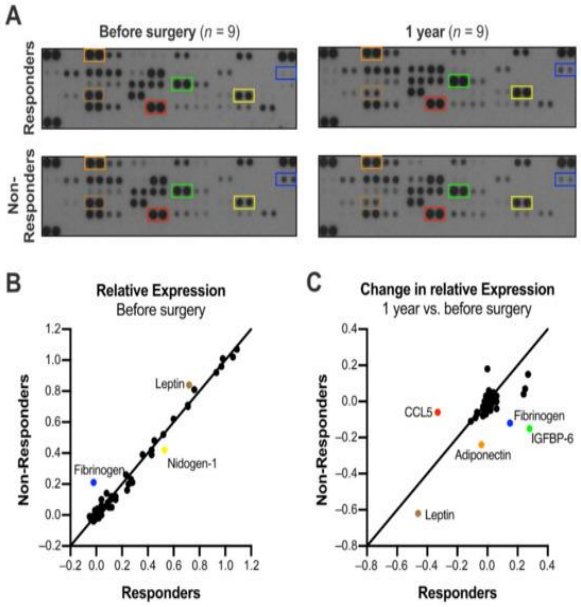

Figure 3. Distinct adipokine signatures in responders versus non-responders

(A) High-resolution scans of the primary array membranes are shown. Serum pools from nine patients in each category were analyzed preoperatively and one year postoperatively.

(B) Quantitative evaluation, normalized to positive control dots, revealed stronger expression of fibrinogen and leptin and lower abundance of nidogen-1 among non-responders.

(C) At the 12-month follow-up, fibrinogen and IGFBP-6 expression rose in the response group but dropped in non-responders. Leptin levels fell more sharply in non-responders, resulting in comparable values between groups at one year. Adiponectin expression remained unchanged in responders, whereas in non-responders it decreased by 23.9% over the same period. Conversely, CCL5 stayed stable in non-responders but declined in patients who benefited from surgery. Color-coded boxes in panel (A) correspond to each protein's location on the arrays.

Furthermore, the sharper leptin reduction in non-responders led to near-equivalent expression across both cohorts by the end of the follow-up. In contrast, adiponectin remained steady among responders but fell significantly (−23.9%) in non-responders within the first postoperative year. Cytokine array analysis also showed that, before surgery, CXCL12, plasminogen activator inhibitor 1 (PAI-1), and macrophage migration inhibitory factor (MIF) were expressed at lower levels in the non-responder subgroup **(Figure S3)**.

Discussion

This study provides insight into the longitudinal behavior of ccK18 levels and highlights its applicability for monitoring liver health in patients undergoing Roux-en-Y gastric bypass. To our knowledge, it represents the largest single-center investigation in which all surgeries were conducted by the same surgeon. A notable reduction in ccK18 concentrations was observed six months postoperatively, consistent with previously published findings [23].

The elevated preoperative ccK18 levels and their pronounced decline after surgery underscore the burden of liver pathology in this bariatric cohort. Despite the absence of formal chronic liver disease diagnoses, most participants likely exhibited NAFLD. According to the NAFLD fibrosis score, approximately 21% had advanced fibrosis prior to surgery. The high ccK18 values alongside established fibrosis metrics, such as the NFS, suggested advanced liver disease in a subset of patients. Therefore, careful evaluation and implementation of non-invasive biomarkers are essential for accurate diagnosis, ongoing surveillance, and timely therapeutic interventions in this population.

Previous studies have noted limitations in using ccK18 as a standalone marker for NAFLD. While combining it with liver stiffness measurements and other biomarkers appears promising [25,37], ccK18 alone has often shown only modest diagnostic accuracy [38,39]. Moreover, precise cut-off values for ccK18 remain undefined, as emphasized by Kwok *et al.* [28]. In this study, we addressed this limitation by monitoring individual ccK18 trajectories over time. Since ccK18 release reflects hepatocyte apoptosis, a central mechanism in metabolic liver disease, it may more accurately mirror disease progression than conventional histological classifications [23-25]. Given the dense, repeated pre- and postoperative monitoring, histological confirmation of steatosis or fibrosis was not performed. Previous work by Vuppalanchi *et al.* demonstrated that reductions in ccK18 correlate with histologic improvement in NAFLD [31]. However, in an unselected cohort without baseline NAFLD screening, absence of ccK18 reduction may simply reflect initially mild liver disease. Indeed, 6 of 9 non-responders had baseline ccK18 <200 U/l, while 13 of 30 responders also had similar starting levels, with no significant difference between groups.

Serial ccK18 measurements identified patients who did not respond to bariatric surgery, defined by <10% reduction at one year postoperatively, consistent with previous reports [8]. Considerable effort was made to minimize variability: all patients underwent a standardized single-center treatment, with RYGB performed by the same experienced surgeon. Nonetheless, postoperative responses varied widely. Potential contributors such as insufficient waist reduction, elevated glucose, and insulin

resistance have been proposed [40-42]. In this cohort, however, weight loss and HbA1c levels did not differ significantly between responders and non-responders, indicating that additional factors drive the variable liver response. More studies are needed to clarify these mechanisms. While ccK18 integration into routine laboratory panels facilitated monitoring, it did not improve predictive accuracy for final outcomes.

Differences in adipokine expression suggest promising avenues for future research. Fibrinogen levels were higher in non-responders, and C-reactive protein tended to be elevated, hinting at systemic inflammation. In responders, fibrinogen rose over the year, while it decreased in non-responders. Postoperative changes in hemostasis may confound fibrinogen's utility as an inflammatory marker [43]. Leptin was also elevated in non-responders. Although findings are mixed, meta-analyses link higher circulating leptin with NAFLD severity, providing a potential explanation for disease persistence in non-responders [44]. Adiponectin levels were similar preoperatively between groups, but decreased in non-responders. Prior studies have shown that adiponectin negatively correlates with insulin resistance, visceral adiposity, advanced fibrosis, and NASH progression [45–48]. More frequent adiponectin measurements could clarify its predictive potential in bariatric surgery outcomes.

In conclusion, this study demonstrates that ccK18-based monitoring is feasible and effective for tracking liver disease progression in bariatric patients. Widespread NAFLD surveillance will rely on non-invasive markers, and we prioritized frequent ccK18 measurements over histology, given its established correlation with liver pathology. By documenting the first-year postoperative trajectory of ccK18, this study lays groundwork for integrating this marker into routine clinical practice. Future research should evaluate the impact of comorbidities, medications, and the predictive value of biomarkers for individual patient outcomes, rather than relying solely on liver biopsy as a reference.

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Ethics statement: None.

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